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Original Research Article

Superior Mesenteric and Renal Flow Patterns During Intraortic Counterpulsation.

Running Title: IABP Physiology

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Abstract

A number of previous studies have shown that blood flow in the visceral arteries is altered during IABP treatment. For these reasons, we utilized a porcine model to specifically analyze the flow pattern of blood into the visceral arteries during IABP use. For this purpose, we measured the superior mesenteric, right renal and left renal flows before and during IABP support, using surgically-placed flowmeters surrounding these visceral arteries. The superior mesenteric flow significantly decreased in early diastole ($p < 0.001$) and in mid diastole ($p = 0.003$ vs. early diastole) whereas in late diastole it increased again ($p < 0.001$ vs. mid-diastole). During systole, the flow was not significantly increased, compared to late diastole ($p = 0.51$) but it was significantly lower than at baseline (both < 0.001). Flows did not differ between right and left kidneys. Perfusion of either kidney did not change significantly at early diastole ($p > 0.05$) whereas it significantly decreased at mid-diastole ($p < 0.001$) raising dramatically at late diastole ($p < 0.001$) with an additional slight increase in systole ($p = 0.054$). This study provides important insights with regards to abdominal flows during intraortic pump counterpulsation. Furthermore, it supports the need to re-think the balloon design to avoid visceral ischemia during circulatory assistance.

New Findings

Visceral ischemia remains one of the majorly feared complications during the use of the intraaortic balloon pump. Employing an animal model, we directly measured the flows at the abdominal level and examined flow patterns during IABP. We show that there is a significant balloon-related reduction in superior mesenteric flow in both early and mid-diastole.

Introduction

Over the past fifty years intra-aortic balloon pumps (IABP) have been widely used to support the failing heart under various pathophysiological conditions. This assist device has been employed in high risk patients after acute myocardial infarction and cardiogenic shock, as previous studies have shown a positive impact on both cardiac output and coronary perfusion (Lorusso et al., 2010).

Diminished blood flow to the visceral arteries, including the mesenteric artery, is, however a known complication of IABP use (Christenson et al., 2002). Despite this evidence, little is known about visceral flow during counter pulsation. Therefore, the aim of the present study was to investigate the flow pattern of the blood into the visceral arteries during IABP treatment.

Materials and Methods

Ethics and Animal Care

The study was approved by the Institutional Animal Welfare Committee of the University of Maastricht, The Netherlands under project number 2013-078 (Dier Experimenten Commissie DEC).

The principal investigators (S.G. and P. L.) were responsible for the animal welfare and carried out all the experiments according to the “Guide for the Care and Use of Laboratory Animals” (Institute of Laboratory Animal Resources, National Research Council-revised 1996) and European Union Directive 2010/63/ on the protection of animals used for scientific purposes. All experiments were carried out with the supervision of the Institutional Animal Welfare veterinarian.

Experimental Protocol

Eight landrace pigs (mean weight 84 ± 6 Kg) were used for this study. Animals were premedicated with intramuscular 10 mg/kg Ketamine (Alfasan, Woerden, the Netherlands), 0.4 mg/kg Midazolam (Actavis, Munich, Germany), and 0.05 mg/kg Atropine (Centrafarm B.V, Etten-Leur, the Netherlands). Anesthesia was induced by intravenous injection of 4 mg/kg Thiopental (Rotexmedica GmbH, Trittau, Germany) and maintained using an intravenous bolus of 0.5 mg/kg Midazolam,

followed by a continuous infusion of 0.5-0.6 mg/kg/h. Analgesia was achieved using a 5 µg/kg bolus Sufentanil citrate (Hameln pharmaceuticals GmbH, Hameln, Germany), followed by a continuous infusion at 6-7 µg/kg/h. Muscle relaxation was provided by infusion of 0.1mg/kg/h Pancuronium bromide (Inresa Arzneimittel GmbH, Freiburg, Germany). Animals were maintained under complete anesthesia throughout the experiment and sacrificed using Euthasol 20% when the experiment was completed (Pentobarbital 150mg/kg, AST Farma B.V., Oudewater, the Netherlands).

Catheters were inserted into the common carotid artery and external jugular vein for measurement of arterial (AP) and central venous (CVP) pressures respectively. A median laparotomy was performed and the visceral vessels were accessed after opening of the peritoneal cavity. Three distinct flow probes (Transonic Systems Inc, Ithica, NY, USA) were placed on the left and right renal arteries and also on the superior mesenteric artery after isolation of these vessels.

After baseline measurements, an 8 Fr./ 40 ml balloon catheter (XEMEX, Zeon Medical Inc, Tokyo, Japan,) was sheathlessly placed in the aorta through the right femoral artery and animals were administered heparin to achieve a minimal activated clotting time of 180 seconds.

Fluoroscopy was performed to confirm correct positioning of the balloon in the aorta and to ensure the balloon did not occlude access to the superior mesenteric artery. The balloon was connected to a Datascope System 97 console (Maquet/Datascope Corp., Fairfield, NJ, US) for control.

Monitoring

During the experiment, electrocardiogram (ECG) monitoring was performed using a standard 5-lead ECG. AP, CVP, right and left renal flows, as well as superior mesenteric artery flow were continuously recorded and acquired at 1000 Hz using a computer-based data acquisition and analysis system (Power Lab 16SP hardware and Lab Chart 7 software; AD Instruments, Sydney, Australia). The Most-Care TM monitoring system (Release 1.0 A, Vytech Healthcare, Padua, Italy) which utilizes the arterial pressure signal to determine numerous cardiac parameters, by employing the pressure recording analytical method (PRAM) determined Stroke Volume (SV), Cardiac Output (CO)

and Systemic Vascular Resistances (SVR) (Scolletta, Romano, Biagioli, Capannini, & Giomarelli, 2005). This method is a clinically validated system for cardiac work estimation which describes hemodynamic performance in terms of the ratio between the hemodynamic work performed and energy expenditure (Onorati et al., 2013; Romagnoli et al., 2009; Romano, 2012).

Flow Measurement protocol

Measurements were taken before inserting the balloon (baseline), after inserting the balloon, but with the balloon off (balloon off), and with the balloon on and set to a ration of 1:1 (IABP, balloon on). The appropriate functioning of the IABP was confirmed by observing significant rises in CO, SV and dP/dT_{max} during counterpulsation (**Table 1**). A schematic of the IABP inflation time-course when compared to the cardiac cycle is shown in **Figure 1**.

For each experimental timepoint, 40 cardiac cycles were taken into account. By synchronizing the flow curve with the peripheral artery wave, ECG and CPV wave, the diastole was divided into 3 phases: 1) early diastole, from the dicrotic notch in the AP tracing to the slight CVP rise before the mitral opening (v-wave); 2) mid-diastole, from the y-descent of the CVP to the P wave at ECG; 3) late diastole, from the beginning of the P wave to the Q wave at ECG. Systolic flow was measured in correspondence of the ECG QRS complex (**Figure 1**). For each timepoint, the mean value (over 40 cycles) of early diastolic, mid-diastolic, late diastolic, and systolic flows were reported. Furthermore, diastolic and systolic areas of the AP were calculated over 40 cycles and the means compared. Moreover, mean flows were indexed by MAP, CVP and driving pressure (MAP-CVP).

Finally, the following parameters were evaluated from arterial samples: Hematocrit (Hct), pH, Base excess (BE), cardiac Troponin I (cTnI) and lactates, using a Vet Scan i-STAT 1 Handheld Analyzer (Abaxis North America, Union City, CA, USA).

Statistical Analysis

Statistical power for the planned sample size was determined by Graph Pad Stat Mate software, release 2.00 (Graph Pad Prism Software, Inc, San Diego, CA) on the basis of the following

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assumptions: type I error of 0.05 (two-sided) and difference in diastolic mesenteric flow of 13.3 ml/min. The calculated statistical power was 0.80. The Shapiro-Wilk test was used to verify normality of variable distribution. As all data was found to be normally distributed, multiple comparisons were performed by one-way ANOVA or Kruskal-Wallis test, as appropriate; Tukey's and Dunn's test were utilized for post-hoc comparison.

Significance was assumed when the p value was ≤ 0.05 . Analysis was carried out using SPSS v. 22 (IBM Corp., Armonk, NY, USA), R version 3.5.2 (R Foundation for Statistical Computing, Wien, Austria) and MATLAB R2013a (MathWork, Natick, MA). Data are expressed as mean \pm standard deviation; whilst the sample size for each measurement is also reported.

Results

Superior Mesenteric Artery Flow Profile.

Figure 2 A-C shows representative examples of recordings from the superior mesenteric artery at baseline, after balloon insertion (balloon off) and during IABP pulsation (balloon on). Mean values for each cycle phase are reported in **Table 2**. Balloon insertion in itself did not alter mesenteric flow significantly at any stage of the cardiac cycle. However, when the IABP was turned on the flow profile markedly changed with systolic flow amplitude and duration decreased, resulting in a significant reduction of the area under the curve ($p < 0.05$ vs baseline). In early diastole, the monotonic decrease in mesenteric flow observed at baseline was replaced by a secondary surge, which partially compensated the overall decrease in the flow area during this phase. In mid diastole flow profile was initially positive and flatter than at baseline but it finally dipped to negative values (reverse flow), resulting in an overall negative flow value. In late diastole, flow underwent a major surge of amplitude similar to systolic flow and also of longer duration; this resulted in a flow area above the baseline value ($p < 0.001$ vs. baseline and balloon off; $p < 0.001$ vs. mid-diastole).

Mesenteric resistance increased significantly with the balloon on (**Figure 3**).

Left Renal Artery Flow Profile.

Figure 4 A-C shows a representative example of the left renal flow. The left renal perfusion (**Table 3**) did not change significantly at early diastole ($p=0.06$ and $p=0.1$ vs. baseline and balloon off, respectively), significantly reduced at mid-diastole ($p<0.001$ vs. baseline and balloon off; $p<0.001$ vs. early diastole) but rose dramatically at late diastole ($p<0.001$ vs. baseline and balloon off; $p<0.001$ vs. mid-diastole). During systole, the flow was slightly increased when compared to late diastole ($p=0.054$), but it was significantly higher than baseline ($p=0.04$) and balloon off ($p=0.04$). The mean of the areas under curve was significantly different in diastole ($p=0.001$ vs. baseline and balloon off) and in systole ($p=0.005$ vs. baseline and balloon off, respectively).

Right Renal Artery Flow Profile.

Figure 4 D-F displays the right renal flow during a number of beats. The right renal perfusion (**Table 3**) mirrored that of the left kidney with no difference in diastolic flows, diastolic area, systolic flow and systolic area.

Mean and Normalized Flows.

With the IABP on, mean mesenteric artery flow decreased significantly ($p=0.001$, **Figure 5**).

Similarly, flow normalized for MAP ($p=0.01$ vs. baseline), for CVP ($p<0.001$) and driving pressure ($p<0.001$) reduced significantly

Moreover, IABP uniformly increased mean renal flows (**Figure 5**), and flows normalized for MAP, CVP, and driving pressure (all, $p<0.05$ vs baseline).

Laboratory Findings

Laboratory findings are shown in **Figure 6**. There was a borderline significant increase in lactates ($p=0.051$) with a non-significant reduction in PH (0.088) but with a significant reduction in BE ($p=0.001$). No significant changes were observed in troponin levels ($p=0.071$)

Discussion

Since its introduction by Mouloupoulos et al. in 1962 the Intra-aortic balloon pump (IABP) has been the most widely used circulatory assist device in critically ill patients with cardiac disease (Mouloupoulos, Topaz, & Kolff, 1962; van Nunen et al., 2016). Its wide use, however, has been harshly questioned over the last few years, especially by the Shock II trial (Thiele et al., 2013). This has resulted in much debate regarding the use of this assist device that has been recently refreshed by new literature in favor of the use of the IABP use under certain pathological conditions (Deppe et al., 2017; Gelsomino, Johnson, & Lorusso, 2018; Iqbal et al., 2016; Ouweneel et al., 2017, 2017).

The classic concept of intra-aortic balloon counterpulsation, positioned in the descending thoracic aorta through the femoral artery, involves inflation at the onset of diastole, which leads to an increase in coronary blood flow (Gelsomino et al., 2011) and potential improvements in systemic perfusion by augmentation of the intrinsic “Windkessel effect” (Bonios et al., 2010). Deflation occurs at the end of diastole, precisely at the start of isovolumic contraction, which leads to a reduction in afterload (Folland, Kemper, Khuri, Josa, & Parisi, 1985; Parissis, 2007). Although IABP effects are predominately associated with enhancement of LV performance, favorable outcomes have been also described on right ventricular function (Krishna & Zacharowski, 2009).

Several studies have been conducted to assess the physiologic effects of IABP as related to hemodynamics (Kern et al., 1999; Parissis, 2007), coronary circulation (MacDonald, Hill, & Feldman, 1987; Ohman et al., 1994; Parissis, 2007), and myocardial oxygen supply/demand (Nanas et al., 1996; Williams, Korr, Gewirtz, & Most, 1982).

In contrast, the effect of the intra-aortic balloon on visceral flow has been poorly investigated. IABP utilization has been associated with balloon-related mesenteric ischemia and ischemic colitis (El-Halawany, Bajwa, Shobassy, Qureini, & Chhabra, 2015; Rastan et al., 2010), and this has also been observed when the balloon was “non-obstructive” and correctly positioned (Byon et al., 2011; Rastan

et al., 2010). Therefore, better insights are required into visceral flow during counterpulsation to achieve the best and safest results.

The objective of this study was to investigate abdominal blood flow during IABP support. For this purpose, we utilized a pig model, and measured the superior mesenteric, right renal and left renal flows before and during IABP support, using surgically-placed flowmeters. As far as we know, there are no reports that have previously measured the flows of the mesenteric and renal arteries simultaneously using three flow probes during counterpulsation.

In our experience, we observed a significant reduction in superior mesenteric flow in early diastole, with flow reaching the lowest values in mid-diastole. Interestingly, in late diastole it re-increased sharply with a slight raise during systole without reaching baseline values. Mean flow was, however, reduced, therefore the late diastolic peak does not compensate the early and late diastolic decrease.

The mechanisms of physiological regulation of the mesenteric flow are based on three main factors: intrinsic (local metabolic and myogenic), extrinsic (autonomic nervous system), and humoral (local or circulating vasoactive substances) (Harper & Chandler, 2016). The presence of the balloon in the vascular stream might interfere with the intrinsic autoregulation. This mechanism, apart from a metabolic control based on the balance between oxygen supply and demand, seems to have a myogenic control aspect with vessels contracting and increasing their tone in response to an increase in transmural pressure. The diastolic inflation of the balloon would lead to an increase in transmural pressure within the mesenteric artery and increased stretch in the arterial wall, leading to local vasoconstriction. This would be mediated through opening of mechanosensitive cation channels, principally sodium (Na^+). The resulting depolarization would activate voltage-gated calcium (Ca^{2+}) channels elevating intracellular Ca^{2+} concentrations, thereby inducing smooth muscle contraction (Harper & Chandler, 2016). This would be confirmed by the evidence, from our findings that when the total mesenteric flow is indexed by vascular resistance, it increases with the balloon on, showing an inverse relation with resistances.

Furthermore, the IABP has effect on aortic baroreceptor output and resultant changes in reflex neurohumoral circulatory control that results to be dramatically altered: diastolic pressure augmentation produces a biphasic output and accentuated diastolic output volley (normally absent), resulting in a net increase in baroreceptor output responsiveness to balloon inflation pressure and inflation-deflation timing (Weber & Janicki, 1974).

The underlying mechanisms leading to increases in late diastole remain to be explained. We could, however, postulate that it is linked to the balloon expansion and to the energy stored in the elastic aortic wall and transmitted back, in late diastole, to the column of blood interposed between the arterial wall and the balloon surface.

In the present study healthy pigs were used which may limit extrapolation regarding mechanisms of decreased mesenteric flow in cardiogenic shock. Since the decrease in flow to the mesenteric is about 20%, it is unclear if this is enough to precipitate mesenteric ischemia. However, we did observe a reduction in base-excess ($p=0.001$), and a borderline significant increase in lactates. Classically, patients with mesenteric ischemia have metabolic acidosis, an elevated D-dimer and elevated serum lactate. (van den Heijkant, Aerts, Teijink, Buurman, & Luyer, 2013)

Nevertheless, these changes are associated with late-stage mesenteric ischemia with extensive transmural intestinal infarction, body tissue hypoperfusion, anaerobic metabolism and death. Therefore, it is perhaps not surprising that the flow reduction observed by us is not associated with a clear metabolic acidosis. Future studies should investigate changes over a more chronic period of time.

Moreover, we confirmed that IABP increases renal flow (Sloth et al., 2008) and this improvement occurred without any difference between the right and left kidneys despite their different anatomical features. However, it is known that there are no differences in diameter or distances to branching between the right and left renal arteries (Tarzamni et al., 2008).

However, similarly to the mesenteric, we found a mid-diastolic decrease and a late diastolic raise that can be explained as reported above. However, in contrast to mesenteric flow, renal flow appeared to be independent of changes in MAP, CVP and driving pressure. Thus, its post-IABP enhancement was not secondary, either to perfusion pressure and resistances in the renal district or to cardiac output. In pigs, renal blood flow is normally maintained through autoregulation until the mean arterial pressure (MAP) is at least 60 mmHg (Wentland et al., 2012). In our experiments, the MAP was >60 mmHg in all animals, therefore the auto-regulatory mechanism as a cause of enhanced kidney perfusion can be excluded. Therefore, it would seem to be directly related to the mechanical effects of the IABP. Thus, the question arises: why the mechanical effect of the IABP rises the renal flow whereas reduces perfusion in the mesenteric artery. Apart from the specific myotonic mechanism described above, it could be related to the short distance between the tip of the balloon and the mesenteric branching and to the flow alterations described just beneath the balloon, leading to a reduced perfusion pressure (Lundemoen et al., 2015). Further research is warranted to clarify this finding.

Clinical Repercussions

Our results, and in particular the demonstration of a significant reduction in mesenteric flow during IABP use, may have important repercussions on its clinical application as well as on the design of “new generation” balloons. Indeed, despite improved design and implantation techniques, the incidence of visceral ischemia, leading to irreversible organ damage and unfavorable prognosis, is still not negligible (Rastan et al., 2010). Visceral ischemia has been often attributed to mal-positioning of the balloon or its length mismatch with the thoracic aorta (Swartz et al., 1992). Nonetheless, a high percentage of patients show abdominal organ hypoperfusion also when the balloon is “non-obstructive” and correctly positioned (Byon et al., 2011; Rastan et al., 2010). This suggests that the mechanics of the IABP, rather than the overlap of its distal tip over the origin of the mesenteric artery, are responsible for hypoperfusion. Our experiments showed that the reduction in flow occurred at the beginning of the diastolic phase with the minimum flow rate observed in mid-diastole. In the final part of the diastolic phase it raised sharply even not reaching baseline values.

Besides the issues of dimension and volume of the balloon discussed elsewhere (Gelsomino et al., 2017), we have now shown that the progression of the inflation within the balloon is, probably, another important issue to be considered. In the balloon employed for these experiments, the gas lumen between the inner and the outer tubes is connected with the balloon at the distal end and the gas line inflows the balloon from proximal end towards the distal balloon's tip. The use of helium allows minimization of delay in transport and rapid inflation capabilities as well as lowering the risk of gas embolism. This confirms previous observations showing that there is a hydrostatic pressure gradient of about 20 mmHg from the proximal to the distal end of the balloon responsible of a preferential inflation pattern that began at the proximal tip and progressed distally (Weber & Janicki, 1974).

Another physical effect responsible of this phenomenon might be the co called "bubble-blowing" effect due to the cylindrical or sausage shape of the balloon leading to larger lateral wall pressures. This means that blood can become 'trapped' in the central segment and preferential inflation of the balloon ends, resulting in ineffective volume displacement and pressure augmentation (Weber & Janicki, 1974). Following these observations, triple-segmented and dual-chambered balloons have been designed but these have never found the favor of clinicians.

Although the present study gains important insight into the behavior of abdominal flow during the use of IABP we believe it should also be seen as a call for discussion about the need for a new IABP design - maybe with differing synchronization between the proximal and distal sections

The proximal balloon, synchronized to the aortic notch, with its inflation during diastole would normally increase the pressure difference between the aorta and left ventricle, the so-called diastolic pressure time index (DPTI) and, consequently, the coronary blood flow and the myocardial oxygen supply. At the same time the deflation of the distal part would ensure normal diastolic abdominal flow. The inflation at late diastole of the IABP distal end might increase abdominal flow during systole through the synergistic interaction of two mechanisms: the energy given back by the elastic return of the aorta and a potentially greater "vacuum" effect (larger afterload reduction), due to the deflation of the balloon at level of its distal end. For the same reasons such a design might,

theoretically, improve the net renal flows by avoiding the early- and mid- diastolic decrements and, at the same time, facilitating late diastolic and systolic perfusion.

Study limitations

A number of inherent limitations of this study must also be considered:

Firstly, the celiac trunk was not isolated and surrounded with a probe since it is very short and fragile in pigs and difficult to approach. After a few attempts this procedure was excluded as a potential risk for animal survival due to the high challenging experimental design.

Secondly, we did not calculate the oxygen consumption in the abdominal circulation as we did not have a catheter directly in the mesenteric vein. This will, however, be the subject of further research.

Thirdly, we did not perform a computed tomography (CT) scan which would have provided more accurate information about the proximal and distal balloon tip position in relation to all visceral arteries. Furthermore, the distance from the end of the balloon to the mesenteric artery was not recorded and, therefore, we were not able to say whether or to what extent a gap existed between the distal part of the balloon and the celiac trunk which may affect both the flow rate and the pattern.

Fourthly, in this study, we used mean arterial pressure as a surrogate measure of organ perfusion pressure. A more accurate measurement on single visceral vessels would allow its precise estimation. For this purpose, we are currently testing a custom-made device for continuous measurement of perfusion pressures in the specific abdominal arteries of interest to gain further insights. Finally, the pathophysiological mechanisms underlying the reduced visceral flow remain unknown. Ongoing in-vitro studies will help gain more information regarding flow characteristics below the balloon (laminar, turbulent, transitional?) and to elucidate whether the type of flow is linked to the balloon effect on visceral circulation.

Conclusions

This study has demonstrated the alterations seen with regards to abdominal flows during intraortic pump counterpulsation and supports the need of re-thinking the balloon design to avoid visceral ischemia during circulatory assistance. Further research will provide more information eventually confirming or rejecting our findings.

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Disclosures

No conflicts of interest, financial or otherwise, are declared by the authors

Author Contributions

SG, JM. and DMJ were involved in conception and design of the research. SG, PL, DMJ, MdJ, OP, MM, FM and FL were involved in acquisition and analysis of the data as well as contributing to drafting and revising the final manuscript. All Authors approved the final version of the manuscript.

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Table 1. Hemodynamics

	Baseline	Balloon Off	Balloon On
HR (beats/min)	100.3±30.2	99.1±29.8	101.7±30.4
SAP (mmHg)	129.1±32.9	128.2±31.5	106.8±30.6 ^{*†}
DAP (mmHg)	70.3±24.2	69.8±23.5	87.4±22.1 ^{*†}
MAP (mmHg)	89.4±13.1	88.7±12.8	92.4±12.3 ^{*†}
SV (ml/min)	58.3±11.3	58.5±11.4	67.6±12.8 ^{*†}
CO (l/min)	5.9±0.8	5.8±0.8	6.9±1.1 ^{*†}
SVR (dyn*s/cm⁵)	1236±235	1302±251	1073±204 ^{*†}
dP/dT_{MAX} (mmHg/sec)	1.18±0.23	1.17±0.22	1.31±0.28 ^{*†}

Abbreviations: HR: Heart Rate; SAP: Systolic Arterial Pressure; DAP: Diastolic Arterial Pressure; MAP: Mean Arterial Pressure; SV: Stroke Volume; CO: Cardiac Output; SVR: Systemic Vascular Resistance; dP/dT_{MAX}: Maximal Pressure/Time Ratio;

* Significance vs. Baseline; † Significance vs. Balloon Off.

Table 2. Superior Mesenteric Flow (ml/min).

	Baseline	Balloon Off	Balloon On
Early Diastole	1341±234	1479±266	273±49 ^{*†}
Mid Diastole	881±163	994±189	-196±33 ^{*†‡}
Late Diastole	698±133	771±131	2024±384 ^{*†‡}
Diastolic Area (mL)	6.87 ± 1.32	6.97 ± 1.68	5.35 ± 1.05 ^{*†}
Systole	2890±564	2845±559	2117±343 ^{*†}
Systolic Area (mL)	8.07 ± 1.58	7.93 ± 1.52	6.15 ± 0.22 ^{*†}

Data is shown as mean± SD. * Significance vs. Baseline; † Significance vs. Balloon Off; ‡ Significance vs. Early- and Mid-Diastole; # Significance vs. Late Diastole

Table 3. Renal Flow (ml/min).

	Baseline	Balloon Off	Balloon On
Left Kidney			
Early Diastole	421±81	389±74	383±72
Mid Diastole	344±69	338±65	198±37 ^{*†‡}
Late Diastole	295±57	281±51	671±129 ^{*†‡}
Diastolic Area (ml)	1.73 ± 0.30	1.92 ± 0.40	2.93 ± 0.62 ^{*†}
Systole	587±103	569±96	715±118 ^{*†}
Systolic Area (ml)	2.05 ± 0.43	2.07 ± 0.37	3.17 ± 0.48 ^{*†}
Right Kidney			
Early Diastole	437±78	387±71	342±65
Mid Diastole	361±69	346±59	239±43 ^{*†‡}
Late Diastole	324±60	284±53	668±131 ^{*†‡}
Diastolic Area (ml)	1.63 ± 0.30	1.68 ± 0.33	2.87 ± 0.58 ^{*†}

Systole	589±113	587±105	711±124 ^{*†#}
Systolic Area(ml)	2.12 ± 0.38	2.10 ± 0.35	3.22 ± 0.47 ^{*†}

Data is shown as mean± SD. * Significance vs. Baseline; † Significance vs. Balloon Off; ‡ Significance vs. Early- and Mid-Diastole; # Significance vs. Late Diastole

Figure Legends

Figure 1. Schematic diagram illustrating the ECG cycle, aortic pressure and mesenteric flow (from top to bottom), during IABP counter pulsation. In the aortic pressure schematic, the solid line curve is the pressure during the counter pulsation and the dashed curve is pressure without counter pulsation. The mesenteric flow curve is shown only during counter pulsation.

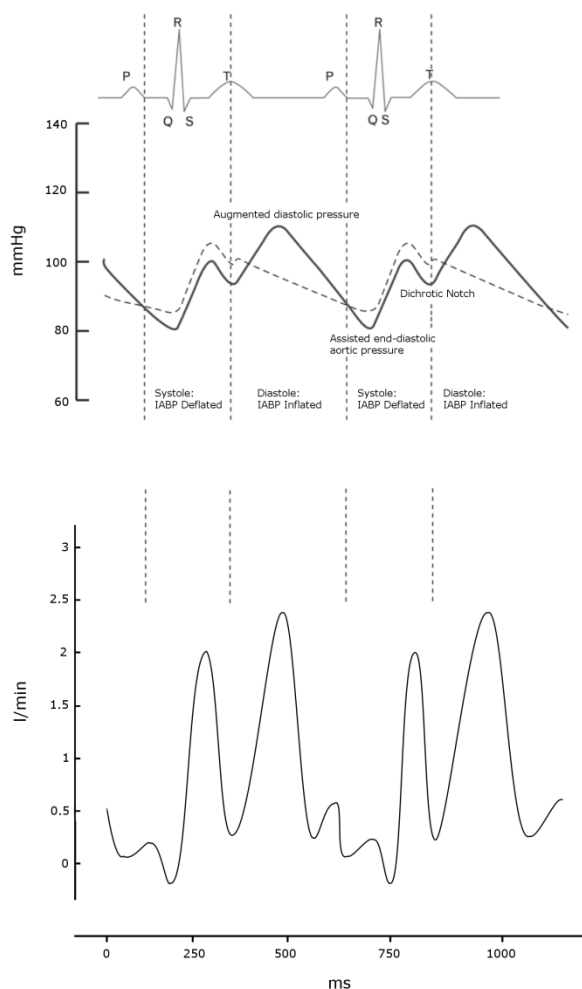


Figure 2. A representative example of the Mesenteric flow. **A.** Without the intraortic Balloon. **B.** With the aortic Balloon inserted and switched off. **C.** With the intraortic Balloon on.

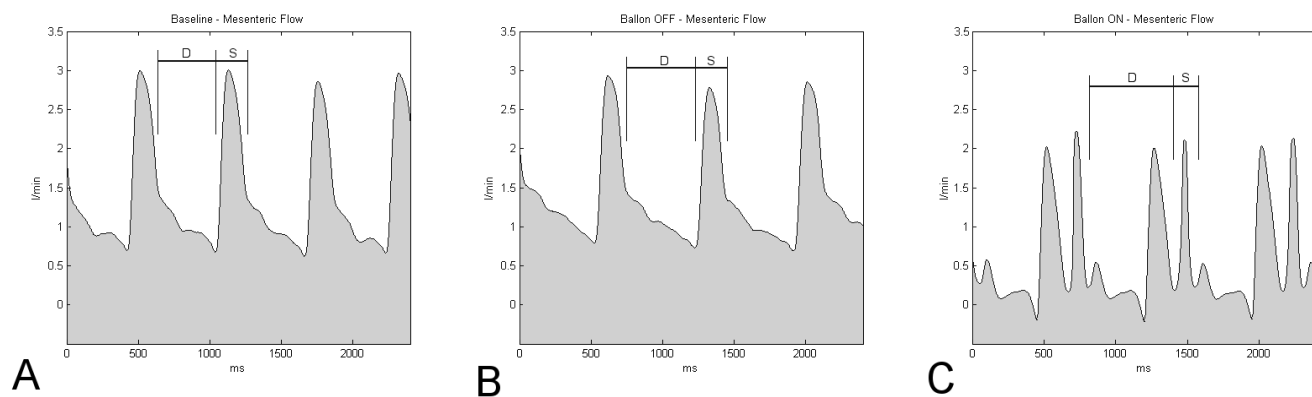


Figure 3. Box and Whiskers plot of the mesenteric resistances under baseline conditions and with the aortic balloon on and off. Each point represents an individual measurement (n=40 points per animal from n=8 animals) *P<0.001 vs. baseline and vs. balloon off.

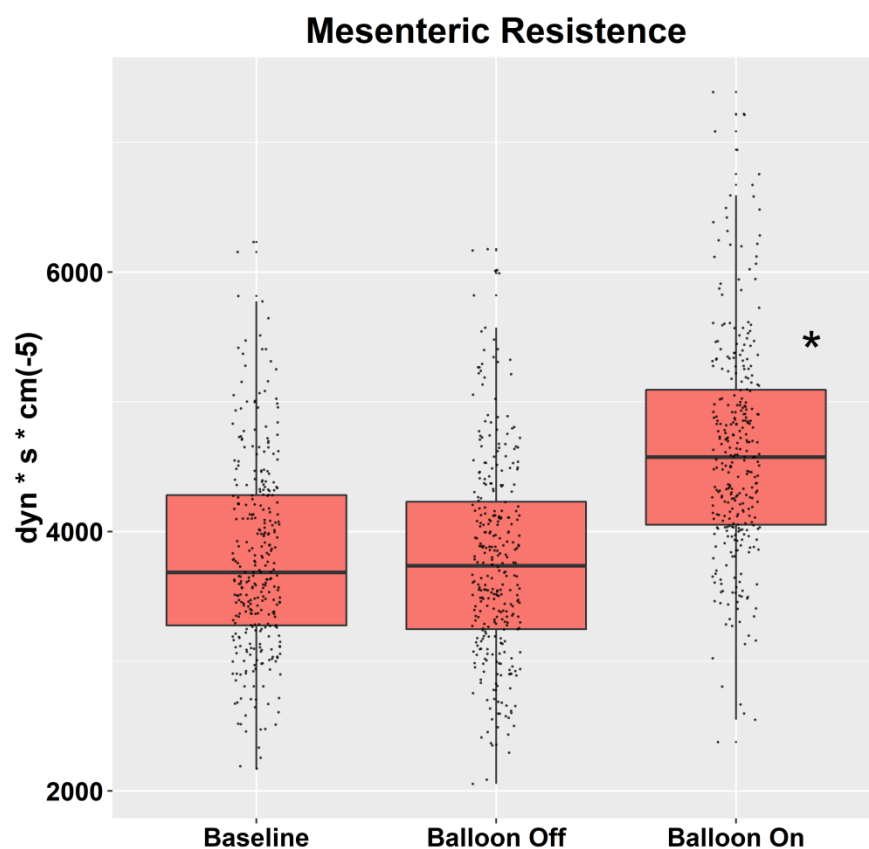


Figure 4. A representative example of the Left and Right Renal flow. In red, the counter pulsed aortic wave. **A.** Without the intraortic Balloon. **B.** With the aortic Balloon inserted and switched off. **C.** With the intraortic Balloon on. **D.** Without the intraortic Balloon. **E.** With the aortic Balloon inserted and switched off. **F.** With the intraortic Balloon on.

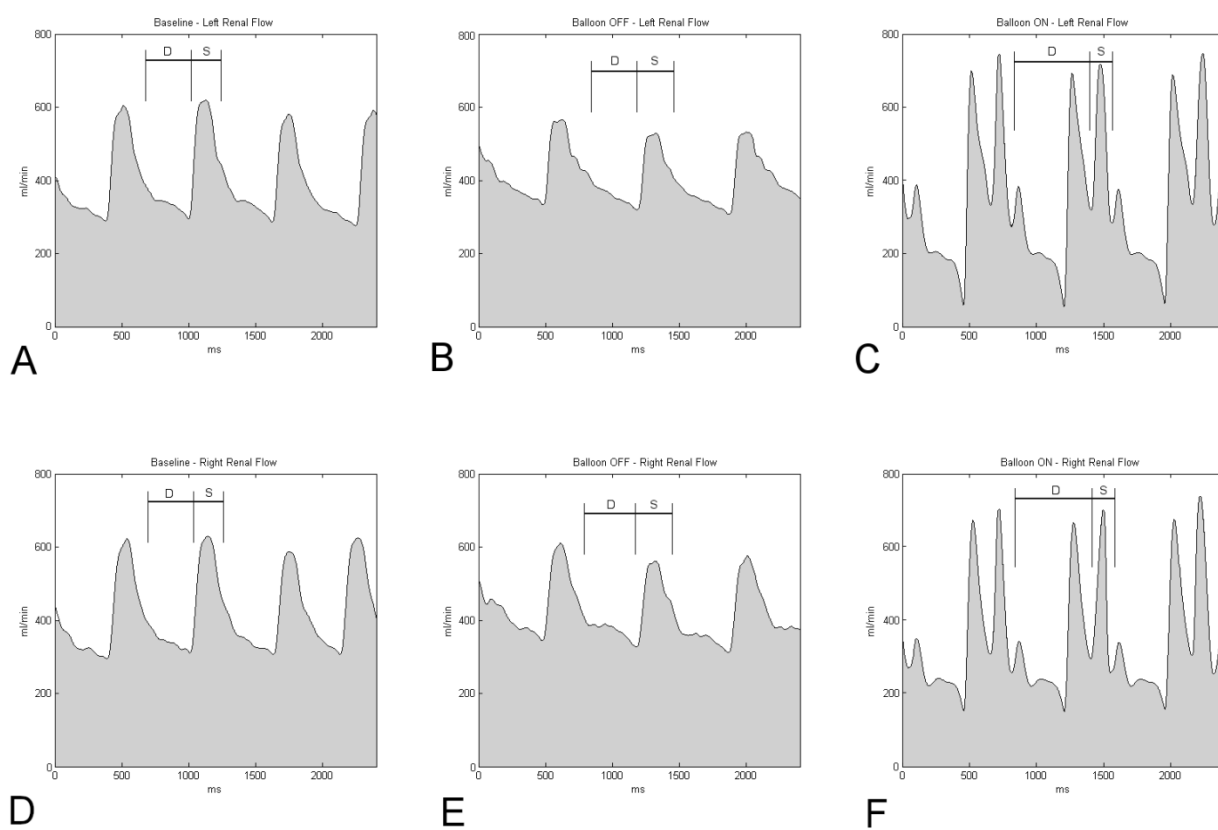


Figure 5. **A.** Mean Mesenteric Blood Flow (MBF), Left Renal Blood Flow (LRBF) and Right Renal Blood Flow (RRBF). The same flows indexed by **B.** Mean arterial pressure (MAP) **C.** Central Venous Pressure (CVP) **D.** Driving Pressure. Each point represents an individual measurement (n=40 points per animal from n=8 animals) * $P < 0.05$ vs. baseline and vs. balloon off.

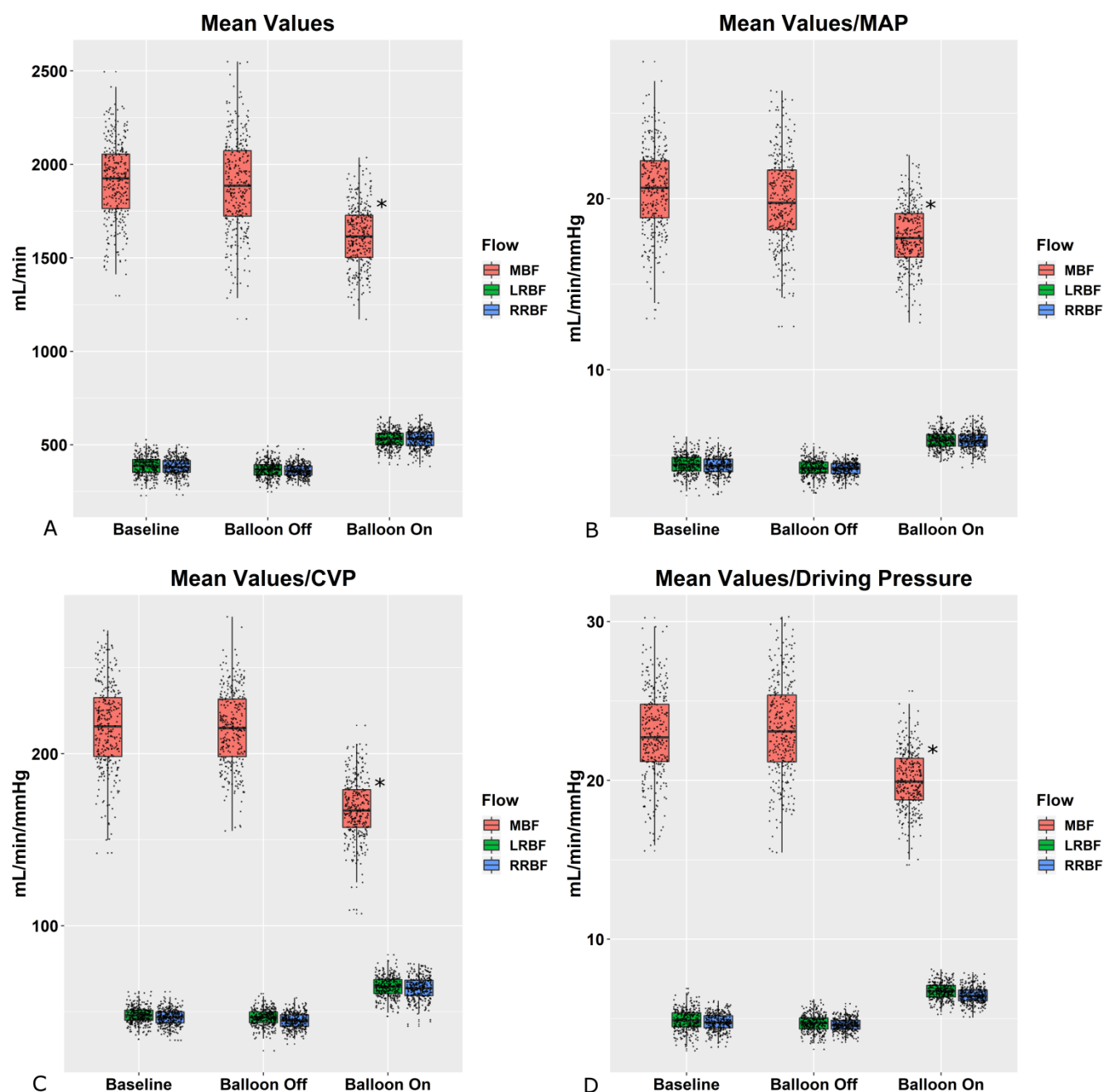


Figure 6. Blood values of various markers. **A.** pH. **B.** Base excess. **C.** Troponin **D.** Serum Lactates. *

P<0.05 vs. baseline and vs. balloon off.

